

Appl. No. 10/091,912

~~Amended February 9, 2006~~

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REMARKS**Status of the Application.**

Claims 1, 19, 28, 30-31, and 33-50 are pending in the application. Applicants reserve the right to file further continuation applications on any subject matter disclosed in the instant application or on the subject matter of any previously or presently cancelled claim. Claims 1, 19, 28, 30, 39, 42 and 49 have been amended herein. Claims 1, 28, 39 and 42 have been amended to more clearly state the metes and bounds of the claim. Claims 19, 28 and 30 have been amended to correct typographical errors. Claim 49 has been amended to clarify the claim without altering the scope thereof. Applicants assert new matter has not been introduced by the amendment.

Claim Objections.

Claims 1 and 28 are objected to as grammatically incorrect as reciting "the residue position corresponding to sites" or "the residue positions corresponding to site". Applicants respectfully point out the claim 1 in the previous amendment had removed the "s" from "sites". Similarly, claim 28 had been amended to remove the "s" from "positions". Applicants do acknowledge that the strikethrough was difficult to see however Applicants believe no further correction is needed. Withdrawal of the objection is respectfully requested.

Claims 28 and 30 are objected to as reciting "SEQ ID NO:-2". Applicants have amended the claims to remove the improper sequence identifier. Withdrawal of the objection is respectfully requested.

35 U.S.C. §112, first paragraph.

Claims 1, 19, 31, 34-41, 44 and 46-50

Claims 1, 19, 31, 34-41, 44 and 46-50 stand rejected under 35 USC §112, first paragraph as failing to be described in the specification. Specifically, the Examiner asserts that the specification, claims or drawings as originally filed fail to describe a variant that has a mutation at either position 192 (Claim 1 and claims dependent therefrom) or position 194 (Claim 39 and claims dependent therefrom) as having increased polyesterase activity and enhanced

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thermostability. Emphasis in original; see page 5 of the Office Action. Applicant respectfully traverses.

Initially, Applicants once again note that SEQ ID NO:2 contains a leader peptide and is numbered beginning at the initiating methionine. The mature sequence, after cleavage of the leader peptide (14 amino acid residues) begins at the alanine in position 15 (*i.e.*, Ala 15 represents the first residue in the protein). Therefore, Phe 180 in the Claims refers to Phe 194 in Figure 18 and SEQ ID NO:2. Thus, the Examiner may be looking for 194 in the specification but should be looking for 180. If the Examiner would find a substitute Sequence Listing to be helpful, Applicants would be happy to provide a new Sequence Listing that includes a sequence that omits the leader peptide.

Applicants have amended Claim 1 to more clearly describe what is considered the invention. The currently pending claim now requires increased polyesterase activity and/or enhanced thermostability. Support for this can be found, for example, in Tables 1 and 3 where variants having a substitution at residue 192 show an increased polyesterase activity and both increased polyesterase activity and enhanced thermostability, respectively. Similarly, Tables 1, 2 and 3 provide support for the 194 residue.

Applicants respectfully request withdrawal of the rejection.

Claims 1, 19, 28, 30-31 and 33-50

Claims 1, 19, 28, 30-31 and 33-50 stand rejected under 35 USC §112, first paragraph as allegedly containing subject which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant respectfully traverses.

Although Applicants must respectfully disagree with the Examiner's assertion, in order to further their business interests and prosecution of the present application, yet without acquiescing to the Examiner's arguments, Applicants have amended claims 1, 28, 39 and 42 to recite "consisting essentially of" instead of "comprising". Withdrawal of the rejection is respectfully requested.

Claims 1, 19, 28, 30-31 and 33-50

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Claims 1, 19, 28, 30-31 and 33-50 stand rejected under 35 USC §112, first paragraph as failing to be described in the specification. Specifically, the Examiner asserts that the specification does not reasonably provide enablement of all cutinase variants having a substitution corresponding to residues 192, 194, and/or 219 of SEQ ID NO:2. Applicant respectfully traverses.

Applicant must respectfully disagree with the Examiner's argument and rationale that the specification lacks guidance. However, Applicants believe the amendments to Claims 1, 28, 39 and 42 provided for *supra* render this rejection moot as well.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 USC 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

35 U.S.C. §112, second paragraph.

Claims 1, 19, 28, 30-31 and 33-50

Claims 1, 19, 28, 30-31 and 33-50 are rejected under 35 USC §112, second paragraph being indefinite. Specifically, the Examiner asserts the recitation of "wild-type *Pseudomonas mendocina* cutinase" or wild-type *P. mendocina* cutinase" renders the claims unclear. Applicants respectfully traverse.

Definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the art at the time the invention was made. *See, e.g., Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999), "it is well-established that the determination whether a claim is invalid as indefinite 'depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the specification.'" quoting *North Am. Vaccine Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 1579 (Fed. Cir. 1993). *See also, Howmedica Osteonics Corp. v. Tranquil Prospects, Ltd.*, 401 F.3d 1367, 1371 (Fed. Cir. 2005), wherein the Federal Circuit overturned an invalidity decision, concluding that "one of ordinary skill in the art would readily ascertain from the written description of the patents that the "transverse sectional dimension" calls for a two-dimensional measurement."

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Thus, an important consideration is whether the terms in a claim adequately define to one skilled in the art the metes and bounds of the claim. Applicants have provided a definition of "wild-type" on page 6, lines 30-31, of the present application. Therefore, Applicants have provided a definition readily understood by the skilled artisan; the claims are definite. Withdrawal of the rejection is respectfully requested.

Claim 19

Claim 19 stands rejected under 35 USC §112, second paragraph as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that Claim 19 is confusing because there can be no substitution with Ser at position 219 as Ser is the original residue at that position. Applicants gratefully acknowledge the Examiner's attention to detail. The claims as originally filed had the substitution of Gly for the Ser at position 219. Applicants in their Response filed December 20, 2004 unintentionally amended Claim 19 to (incorrectly) cite the substitution as being Ser not Gly. By the current amendment Applicants have corrected this inadvertent error. Withdrawal of the rejection is respectfully requested.

Claim 49

Claim 49 stands rejected under 35 USC §112, second paragraph as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that it is not clear how the variant comprises substitution at position 194 (see page 4 of the Office Action). Applicants respectfully traverse.

Although Applicants must respectfully disagree with the Examiner's assertion, in order to further their business interests and prosecution of the present application, yet without acquiescing to the Examiner's arguments, Applicants have amended the claim to (hopefully) clarify the claim. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §103.

The Examiner has maintained his rejection of claims 1, 28, 30, 33-39 and 41-50 as allegedly obvious over Poulouse, *et al* (US Patent 5,352,594). Applicant respectfully traverses the rejection.

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To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

Thus, a *prima facie* case of obviousness requires the Examiner to cite to a combination of references which (a) suggests or motivates one of skill in the art to modify their teachings to yield the claimed invention, (b) discloses the elements of the claimed invention, and (c) provides a reasonable expectation of success should the claimed invention be carried out. Failure to establish any one of these requirements precludes a finding of a *prima facie* case of obviousness and, without more, entitles Applicants to withdrawal of the rejection of the claims in issue.¹ Applicants urge that the Examiner has failed to establish at least one of the requirements, i.e., a reasonable expectation of success, as discussed below.

Applicants submit that Poulouse *et al.* teach "... one would in general use the crystal structure of the enzyme to determine which amino acids are within 15 angstroms of the active site regardless of the primary structure of the enzyme. Where no crystal structure is available, positions in the primary sequence about 6 amino acids on either side of a catalytic amino acid would be within the 15 angstrom requirement." (Poulouse *et al.*, at col. 5, lines 50-57). Applicants respectfully submit that as the catalytic triad is composed of Ser126, Asp176, and His206 (i.e., positions 140, 220, and 190 of SEQ ID NO:2), there is no teaching nor suggestion in Poulouse *et al.* to modify the amino acid at any of the currently claimed positions in order to increase the polyesterase activity and/or thermostability of the enzyme. The Examiner has acknowledged this assessment (see page 9 of the Office Action).

¹ See e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); and *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

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At best Poulouse *et al.* is an invitation to try. The "obvious to try" standard in determining the patentability is a standard which has been thoroughly discredited. Indeed, an obviousness rejection is inappropriate, where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful." *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 10 USPQ2d 1843, 1845 (Fed. Cir. 1989). For example, there is no direction within Poulouse *et al.* as to which, *if any*, amino acid falling within 6 amino acids on either side of any one of the three residues in the catalytic triad could be replaced with any one of the other 19 amino acids would result in enhanced thermostability and/or polyesterase activity. There is no motivation to select from the $(6 \times 2 \times 3 \times 19 =)$ 684 possibilities provided the currently claimed invention.

Under patent law with regard to obviousness, a reasonable expectation of success is to be assessed from the perspective of one of ordinary skill in the art at the time the invention was made. At the time the invention was made it was well established that altering amino acid sequences could result not only in differences in the expression and secretion levels of the protein but also alter the properties of the protein. It was very likely that altering the amino acids in the catalytic region would result in a decrease in the enzymatic activity or thermostability. This supports Applicants' position that one skilled in the art would not have a reasonable expectation of success in altering the amino acid sequence as presently claimed, e.g., creating the variant I192M, would enhanced thermostability and/or polyesterase activity.

Thus, Applicant respectfully requests that this rejection be withdrawn and the Claims be passed to allowance.

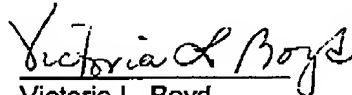
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CONCLUSION

In light of the above amendments, as well as the remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7615.

Respectfully submitted,
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